UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CAMDEN VICINAGE

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION **This Document Relates to All Actions**	MDL No. 2875 Honorable Robert B. Kugler, District Court Judge Oral Argument Requested

DEFENDANTS' MEMORANDUM OF LAW IN OPPOSITION TO PLAINTIFFS' MOTION TO PRECLUDE OPINIONS OF DEFENSE EXPERT DANIEL CATENACCI, M.D.

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Pursuant to Federal Rules of Evidence 104, 403, and 702, Defendants' Executive Committee, on behalf of all Defendants in this litigation, submit this memorandum of law in opposition to Plaintiffs' Motion to Preclude Opinions of Defense Expert Daniel Catenacci, M.D. ("Motion"),[1] and state as follows.

INTRODUCTION

Dr. Catenacci has offered his opinion, as a clinical oncologist and cancer researcher at the University of Chicago, that there is insufficient evidence to support Plaintiffs' claim that NDMA and/or NDEA are carcinogenic to humans at the levels detected in some batches of valsartan, assuming exposure over the period during which those impurities existed. In offering his opinions, Dr. Catenacci undertook an extensive review of the available medical literature and appropriately weighed each study and data point according to accepted scientific hierarchies. His opinions are based on his review and assessment, as well as his education, training and experience as both a treating oncologist and cancer researcher.

Plaintiffs do not contest Dr. Catenacci's qualifications to offer his opinions and do not argue that his opinions would not be relevant or helpful to a jury; consequently, they concede Dr. Catenacci is qualified and his opinions "fit" this

[1]Dr. Catenacci's Expert Report (the "Report") is attached to the accompanying Certification of Seth A. Goldberg, Esq. ("Goldberg Certification") as **Exhibit A**. All Exhibits referenced are attached to the Goldberg Certification unless otherwise noted.

case. Instead, consistent with Plaintiffs' flawed overall approach to general causation, the Motion improperly attempts to reframe the inquiry as whether NDMA and/or NDEA could be carcinogenic at *any* theoretical level, regardless of the lack of such evidence in human studies, let alone the lack of data addressing the trace levels of NDMA/NDEA detected in valsartan and valsartan-containing drugs. Plaintiffs devote much of their Motion to mischaracterizing Dr. Catenacci's testimony on the question of whether NDMA/NDEA might be carcinogenic at some theoretical level not at issue here, setting up a straw man argument that any willingness to contemplate that NDMA/NDEA could be carcinogenic at any level means Dr. Catenacci has somehow "contradicted" his opinions and should be excluded. Plaintiffs' argument is specious and is not based on any cognizable ground for exclusion under Rule 702.

The actual question of general causation before this Court is whether Plaintiffs have carried their burden of proving that NDMA and/or NDEA are carcinogenic to humans at the non-theoretical levels detected in the subject batches of valsartan during the alleged period of potential exposure. *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1242 (5th Cir. 2005) (citing *Science for Judges I: Papers on Toxicology and Epidemiology* 12 J. L. & Pol'y. 1 (2003): "Dose is the single most important factor to consider in evaluating whether an alleged exposure caused a specific adverse effect. Often low dose exposures -- even for many years -- will

have no consequence at all, since the body is often able to completely detoxify low doses before they do any damage. Furthermore, for most types of dose-response relationships following chronic (repeated) exposure, thresholds exist, such that there is some dose below which even repeated, long-term exposure would not cause an effect in any individual"); *In re Abilify (Aripiprazole) Prods. Liab. Litig.,* 299 F. Supp. 3d 1291, 1307-08 (N.D. Fl. 2018) ("for the vast majority of substances, there are threshold doses below which no individual will respond… Consequently, a reliable expert opinion on general causation should address what levels of exposure to a drug increase the risk of adverse effects. Indeed, the expert who avoids or neglects this principle of toxic torts without justification casts suspicion on the reliability of his methodology"); *In re Bextra & Celebrex Mktg. Sales Practices & Prod. Liab. Litig.*, 524 F. Supp. 2d 1166, (N.D. Cal. 2007) (excluding expert opinions that medication could cause claimed harm at lower doses than studied).

Dr. Catenacci's opinion is clear and in no way "contradictory": he has opined, both in his Report and during his deposition,[2] that there is insufficient evidence to support Plaintiffs' hypothesis that NDMA and/or NDEA are carcinogenic at the levels actually at issue in this litigation. And Dr. Catenacci's opinions are well-grounded in medical literature and reliable, accepted methodology.

[2]A copy of Dr. Catenacci's deposition transcripts (with Errata) are attached, collectively, as **Exhibit B**.

Plaintiffs' Motion does not offer any cogent basis under Rule 702 to exclude Dr. Catenacci's relevant and helpful opinions. Plaintiffs' false assertion that Dr. Catenacci failed to consider relevant literature or gave "uneven" treatment to literature on which he relied is based on a deliberate misreading of Dr. Catenacci's testimony and Report, in which he clearly explains the scientific reasoning behind his decision to give more weight to scientific literature directly addressing issues relevant to the general causation inquiry than he gave to evidence that could provide, at best, inferential or analogy-based reasoning. That is a proper methodology and consistent with scientific principles.

Plaintiffs' tortured misreading of Dr. Catenacci's deposition testimony to claim he has somehow contradicted his own opinions likewise supplies no valid grounds for excluding his opinions. Dr. Catenacci's deposition testimony is fully consistent with his opinions, as made plain by other (often immediately adjacent) testimony Plaintiffs fail to mention. Moreover, even accepting Plaintiffs' flawed logic *arguendo*, these manufactured "contradictions" are not grounds for exclusion under Rule 702 or relevant case law; scientific disagreement or purported impeachment is fodder for cross-examination, not exclusion.

Ultimately, Plaintiffs have failed to demonstrate any ground sufficient to exclude (or even limit) Dr. Catenacci's opinions, all of which should be admitted.

LEGAL STANDARD

Federal Rule of Evidence 702 provides that a witness who is "qualified as an expert by knowledge, skill, experience, training, or education" may offer opinions in a case if (i) the expert's "scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue"; (ii) "the testimony is based on sufficient facts or data"; (iii) "the testimony is the product of reliable principles and methods"; and (iv) "the expert has reliably applied the principles and methods to the facts of the case." The Third Circuit has interpreted the specialized knowledge requirement liberally, recognizing that "the basis of specialized knowledge can be practical experience as well as academic training and credentials." *Elcock v. Kmart Corp.*, 233 F.3d. 734, 741 (3d Cir. 2000) (internal quotation marks omitted); see also *Waldorf v. Shuta*, 142 F.3d 601, 625 (3rd Cir. 1998) (same); *In re Paoli R.R. Yard PCB Litig.,* 35 F.3d 717, 741 (3rd Cir. 1994) (liberal admissibility of expert testimony "extends to the substantive as well as the formal qualification of experts").

The requirements of Rule 702 must be applied with the same "'liberal thrust' of the Federal Rules of Evidence and their 'general approach of relaxing the traditional barriers to opinion testimony.'" *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 593 (1993). To be admissible, "the basic minimum is that there must be some scientific validation of the theory advanced by the expert." *Id.*; *Holbrook v.*

Lykes Bros. S.S. Co., 80 F.3d 777 (3d Cir. 1996) ("in placing restrictions on [expert's] testimony because he did not possess the exact background the court deemed appropriate, it erred").

Scientific disagreement is not sufficient grounds for the exclusion of expert testimony and is not for the Court to decide in its capacity as a gatekeeper under Rule 702/*Daubert*. *See, e.g., In re Gabapentin Patent Litig.*, MDL Dkt. No. 1384, 2011 WL 12516763, at *10 (D.N.J. Apr. 8, 2011) (concluding that disagreement between experts regarding application of a methodology presents "a battle of the experts" to be resolved by the trier of fact); *United States v. Grace*, 455 F. Supp. 2d 1196, 1199 (D. Mt. 2006) (Expert testimony even as to disputed evidence is admissible under Rule 702: "It appears that there is some scientific disagreement... It is not the Court's role to settle scientific disputes… it is an issue going to the weight of the evidence, and is best left to the jury"); *see also Broe v. Manns*, No. 15-985, 2016 WL 7048988, at *4 (M.D. Pa. Dec. 5, 2016) ("Any disagreement plaintiffs have with the expert can be dealt with through cross-examination, presentation of contrary evidence and proper jury instructions"); *In re Asbestos Prods. Liab. Litig.*, 714 F. Supp. 2d 535, 544 (E.D. Pa. 2010)(regarding whether an expert "ignored" relevant epidemiological studies, the court found the challenging party was "free to argue credibility to the jury"); *In re Diet Drugs Prods. Liab. Litig.,* MDL No. 1203, 2000 WL 962545, at *13 (E.D. Pa. June 28, 2000) (finding that disagreement with

the methods used by an expert is a question that "goes more to the weight of the evidence than to reliability for Daubert purposes").

As set forth in the following sections, Dr. Catenacci's opinions satisfy all the requirements of Rule 702 and Plaintiffs have not offered any cognizable grounds for excluding those opinions.

ARGUMENT

I. PLAINTIFFS CONCEDE DR. CATENACCI IS QUALIFIED AND THAT HIS OPINIONS "FIT" THIS CASE.

There are three grounds for excluding an expert witness' testimony under Rule 702 – qualifications, methodological reliability, and "fit," or whether the opinions will assist a jury in understanding the scientific issues at bar. Fed. R. Evid. 702; *Yarchak v. Trek Bicycle Corp.*, 208 F. Supp. 2d 470, 496 (D. NJ. 2002); *Magistrini v. One Hour Martinizing Dry Cleaning*, 180 F. Supp. 2d 584, 595 (D.N.J. 2002), *aff'd*, No. 02-2331, 2003 WL 21467223 (3rd Cir. June 25, 2003).

Plaintiffs have not raised any argument that Dr. Catenacci is not qualified to offer the opinions set forth in his Report or that those opinions do not "fit" this case. As such, they have conceded that two of the three possible grounds for exclusion under Rule 702 do not apply. The only possible ground for exclusion urged by Plaintiffs are misguided critiques of Dr. Catenacci's methodology. Critically, however, Dr. Catenacci's qualifications, the nature of his opinions and their fit with this case also make clear why his methodology is sound. Thus, by ignoring Dr.

Catenacci's qualifications and the methodology he employed in arriving at his opinions, Plaintiffs concede reasons why his opinions should not be excluded.

A. Dr. Catenacci Is Qualified To Offer General Causation Opinions On NDMA/NDEA Carcinogenicity.

Dr. Catenacci is a practicing clinical oncologist and a cancer researcher at the University of Chicago, where he completed fellowships in hematology and oncology and in GI Translational Research in digestive malignancies, one of the cancer types identified by plaintiffs in this litigation. *See* Ex. A to the Report ("Catenacci CV") at p. 1; **Exhibit C**, Plaintiffs' Disclosure of Cancer Types. He is the only practicing clinical oncologist to offer opinions, here. He is also an active research scientist, having designed and executed many clinical trial protocols in service of his research, including serving as principal investigator — including national principal investigator — in several trials related to gastric cancer therapies, among others. Catenacci CV, at pp. 18-23.

Dr. Catenacci has also published and taught extensively on subjects relevant to specific cancer types at issue in this litigation, cancer causation, and epidemiology. Indeed, in addition to multiple medical textbook chapters, reviews, editorials and commentaries, Dr. Catenacci is an author on more than 60 peer-reviewed articles, with a primary focus on gastrointestinal cancers and their molecular and genomic origins, treatment options, and prognoses. Catenacci CV, at pp. 2-8. Dr. Catenacci also serves as Associate Editor of the Journal of the American

Medical Association Network Open and the journal Oncology, and on the editorial board and as an ad hoc reviewer on numerous other medical journals. *Id*. at p. 18.

For the past ten years, Dr. Catenacci has also taught medical students at all levels, including a Masters/Ph.D.-level course in Cancer Biology and a medical student course in Epidemiology and Research Design, as well as numerous lectures in specific cancers and treatment paradigms. *Id*. at pp. 23-24.

Without actually arguing Dr. Catenacci is not qualified to offer his opinions or that they are not reliable, Plaintiffs offer a vague criticism that Dr. Catenacci was "barely aware" of the NDMA/NDEA issues in valsartan prior to his engagement in this litigation. Plaintiffs cite authority for the proposition that expert testimony "prepared solely for the purposes of litigation. . . should be viewed with some caution." Motion at 14 (citing *Magistrini v. One Hour Martinizing Dry Cleaning*, 180 F.Supp.2d 584, 594 (N.J. Dist. Ct. 2002)). That is a strained application at best. Dr. Catenacci's opinions are based on his knowledge of cancer research and carcinogenesis. Dr. Catenacci is a cancer researcher who studies numerous cancers including a particular focus on gastric cancer, which Plaintiffs have put at issue. His opinions are based on an extensive review of the literature surrounding the ability of NDMA and/or NDEA to cause cancer. That Dr. Catenacci has not previously researched those two specific molecules in a lifetime of research and authorship on the molecular and genomic origins of cancer does not render his opinions any less

reliable. The question under *Magistrini* is whether the expert's opinions "grow naturally out of research the expert has conducted independent of the litigation," and was one of many factors considered in evaluating reliability. *Id*. Dr. Catenacci's opinions here are an outgrowth of the same principles and methods he uses in his own research, and *Magistrini* does not support their exclusion.

Plaintiffs' reliance on *Player v. Motiva Enterprises,* 2006 WL 166452 (D.N.J. Jan. 20, 2006), *aff'd,* 240 F. App'x 513 (3d Cir. 2007), is similarly misplaced. In *Player,* the court found unreliable the plaintiffs' expert's opinion on diminution in property value, because he failed to consider the actual extent of contamination involved with the property and relied on misleading analogy to inapposite properties. *Id.* at *7-8.[3] Here, Plaintiffs cannot identify any evidence Dr. Catenacci failed to consider. Their complaint is simply that he did not give it the same weight their own experts misapply, which is not a basis for exclusion.

Dr. Catenacci is well-qualified to opine about various cancers, their causes and/or associated risk factors, and prognoses and treatment modalities. Based on his

[3]Plaintiffs' reliance on *Player* and *Mirena*, discussed *infra*, is ironic given their own experts' (i) efforts to explain away in their own reports the key human epidemiology studies involving valsartan, (ii) failure to consider or give any weight to the doses of NDMA/NDEA shown to induce cancer in the animal models on which they rely, and (iii) reliance on analogy to inapposite occupational inhalation exposure to nitrosamines. *See*, *e.g.*, Defendants' Motions to exclude Drs. Lagana, Panigrahy and Etminan. *See* Dkt. No. 1716, 1717, 1718.

extensive experience as a researcher, principal investigator for clinical trials and peer reviewer for leading medical journals, he is also well-qualified to read and interpret scientific literature, assess and critique study design and execution, and testify as to the reliability and relative power of research studies and their scientific conclusions as published in peer-reviewed literature.

B. Dr. Catenacci's Opinions Are Directly Relevant To The General Causation Inquiry Before The Court.

The opinions Dr. Catenacci has offered in this litigation fit squarely within his qualifications and expertise and are directly relevant to the general causation inquiry before this Court. An expert's opinions "fit" the case so long as they will assist the jury, by providing it with relevant information, necessary for a reasoned decision of the case. *Yarchak v. Trek Bicycle Corp.*, 208 F. Supp. 2d 470, 496 (D.NJ. 2002); *Magistrini*, 180 F. Supp. at 595. Dr. Catenacci's opinions unquestionably satisfy this standard.

The full scope of Dr. Catenacci's opinions are set forth in his expert Report and were further explained in his deposition. Briefly, Dr. Catenacci offers opinions that speak directly to the lack of evidence supporting the hypothesis Plaintiffs must prove to establish general causation: exposure to NDMA and/or NDEA at the levels detected in valsartan and for the duration over which those impurities existed could cause the cancers plaintiffs' claim. Report, at pp. 29-47. Plaintiffs have tried to reframe that question to suggest that, so long as there is evidence that NDMA/NDEA

are carcinogenic to animals at doses orders of magnitude higher than found in any valsartan, it should be presumed they are carcinogenic at low doses in humans, based on supposed similarity in their metabolism across species. Dr. Catenacci directly addresses and refutes those invalid theories based on a comprehensive review of the medical and scientific literature on the subject and a clear hierarchical ranking of the quality of that evidence. He also critiques the inappropriate weighting plaintiffs' experts place on that same evidence, such as the relative weakness of plaintiffs' reliance on dietary, animal, and mechanistic studies in the face of epidemiological evidence of humans who were exposed to nitrosamine-containing valsartan. *Id*.

In addition, Dr. Catenacci provides important contextual opinions on the causation evidence from his unique perspective as the sole clinical oncologist offered at this general causation stage.[4]

Specifically, Dr. Catenacci opines that cancer is a blanket term for a set of diseases with differing etiologies that share the common trait of deleterious cell growth. Report, at pp. 4, 6-8. Dr. Catenacci opines on the genetic etiology of cancer and the myriad factors that can cause the genetic alterations that lead to cancer, the number of such alterations or mutations necessary for the formation of a cancer, and

[4]Of course, should any of Plaintiffs' claims avoid disposition at the general causation stage, Dr. Catenacci's opinions as a practicing medical oncologist also will be important to the jury's specific causation analyses.

the inability, in most cases, to identify a specific exposure or insult that caused a mutation in a particular individual. *Id*. He further opines on the incidence rates in the general population and the risk factors associated with each of the cancers plaintiffs have placed at issue. *Id*., at pp. 14-29.

Each of these subjects is relevant to the general causation inquiry and to understanding the evidence available to resolve that inquiry. It is also subject matter within Dr. Catenacci's expertise and professional experience — these are questions he considers, researches, and teaches students how to answer.

Ultimately, by failing to raise any challenge based on Dr. Catenacci's qualifications or the relevance of his opinions, Plaintiffs concede they "fit" this case and appropriately were delivered by Dr. Catenacci.

II. DR. CATENACCI'S METHODOLOGY IN FORMULATING HIS OPINIONS IS RELIABLE.

The sole ground on which Plaintiffs urge Dr. Catenacci's testimony be excluded are supposed inadequacies in his methodology. Plaintiffs support that false charge, however, by mischaracterizing Dr. Catenacci's testimony. Plaintiffs even argue Dr. Catenacci failed to consider studies specifically identified on his List of Materials Considered. *See* Ex. B to Report. In truth, Plaintiffs' gripe is that Dr. Catenacci did not give to certain studies the weight that Plaintiffs' experts improperly ascribe them in support of their own opinions. In each instance, Dr. Catenacci's report and deposition testimony make clear why he considered other

evidence more important and/or rejected plaintiffs' preferred literature as unreliable.

Ultimately, none of plaintiffs' arguments about Dr. Catenacci's methodology amounts to more than unfounded scientific disagreement, which is not a proper ground to exclude or limit Dr. Catenacci's opinions.

A. Dr. Catenacci Appropriately Gave Primary Importance To Human Epidemiology Studies That Address The Question At Issue Here.

It is fundamental that, in personal injury MDLs such as this one, the primary method for answering the general causation question of whether exposure to a particular substance caused a particular disease is an examination of epidemiological evidence associating the exposure with the disease. *See Soldo v. Sandoz Pharms. Corp.,* 244 F. Supp. 2d 434, 533 (W.D. Pa. 2003) (noting "[t]he need for statistically significant epidemiology is particularly acute" in a case where the disease occurs in the general population in order "to determine whether any given case of [the disease] could possibly be attributable to a particular drug"); *see also Magistrini,* 180 F.Supp.2d, at 590 (the focus of epidemiology is general causation, i.e., "is the agent in question capable of causing disease?"); *In re Johnson & Johnson Talcum Powder Prod. Mktg., Sales, Practices & Prod. Litig.,* 509 F. Supp. 3d 116, 157 (D.N.J. 2020) ("Generally speaking, epidemiology is the best evidence of general causation in a toxic tort case") (citations omitted). Plaintiffs' own experts agree this is the "optimal approach." *See* July 4, 2021 Report of Dr. Mahyar Etminan, at 9 ("The optimal approach in assessing the risk of cancer with NDMA and NDEA containing

valsartan is by careful assessment of data from large population based epidemiologic studies.").

Not all epidemiologic evidence is equally impactful, however. Science ranks epidemiological evidence hierarchically — the evidence that most closely examines the question at hand must be given the most weight, while evidence that attempts to answer the question by analogizing data points or by abstraction must be afforded less weight. Report, at p. 38; *See In re Accutane,* 234 N.J. 340, 355 (2018) ("[w]hen ordered from strongest to weakest, systematic review of randomized trials (meta-analysis) is at the top, followed by single randomized trials, systematic reviews of observational studies, single observational studies, physiological studies, and unsystematic clinical observations"), *citing Reference Guide on Medical Testimony,* at 723-24; *Duke v. Honeywell Int'l Inc.,* 2012 Phil. Ct. Com. Pl. LEXIS 122, 78-79 (2012) ("[I]t is generally accepted that there is a hierarchy of studies used to demonstrate a causative relationship between exposure to an agent and development of a disease. Because of the inherent characteristics of the design of the studies, some methods are stronger (more reliable) that others in predicting causation.").

Dr. Catenacci has testified that this is the appropriate scientific methodology and the method he used in formulating his opinions in this case, consistent with his practice as a cancer researcher. Specifically, Dr. Catenacci places the most weight on human epidemiological studies comparing valsartan users exposed to the

NDMA/NDEA impurity against those not exposed to the impurity. Report, at pp. 4; 38; Ex. B at 212:4-11 (testifying that human epidemiological data is "the most relevant data to the question that we're asking"), 217:24-218:9 (testifying that "studies [] looking at surrogate questions using surrogate assessments and estimations of exposure" are "far lower on the hierarchy of evidence" than the human epidemiological data), and 82:2-5 (testifying that he followed the same methodology in this case as he does in his regular research).

As Dr. Catenacci opines and as Plaintiffs concede, there have been two large human epidemiology studies comparing cohorts of individuals known to have been exposed to valsartan containing the NDMA impurity against users of valsartan presumed unexposed to NDMA in valsartan — the studies by Gomm and Pottegard. Report, at pp. 38-40; Ex. B (Catenacci Dep.) at, e.g., 211:20-213:10. Dr. Catenacci appropriately places the most weight on those two human epidemiological studies, because they directly address the general causation inquiry here: did exposure to the NDMA/NDEA impurity in valsartan over the period in which it existed cause any plaintiff's cancer.

As Dr. Catenacci opined in his report and discussed in his deposition, the Gomm study found no increased risk of overall cancer associated with exposure to nitrosamine-containing valsartan. The Pottegard study similarly did not find any statistically significant association between nitrosamine-containing valsartan

exposure and overall cancer or any individual cancer type. The Gomm study provides, at most, weak evidence of an association between exposure to NDMA-containing valsartan and liver cancer; but, critically, not a single subject in the Pottegard study developed liver cancer and other scientific literature similarly fails to support an association with liver cancer. **Exhibit D** and **E** (Gomm and Pottegard)[5]; *see also* Mot. Ex. D.

Plaintiffs critique Dr. Catenacci's reliance on the Gomm and Pottegard studies by claiming he supposedly gave them "uneven" treatment. That is false, but even if it had merit, it would not be a reason to exclude or limit Dr. Catenacci's opinions.

First, Plaintiffs labor to minimize the findings in the Pottegard study, saying that Dr. Catenacci "opined that the increased risk for colorectal cancer (1.46) and the increased risk for uterine cancer (1.81) were entitled to no consideration." Mot., at 8. Dr. Catenacci testified that those findings do not carry scientific significance because that is precisely what the authors of that study concluded themselves — the supposed increased risks had no statistical significance:

> Overall, exposure to potentially (probably or possibly) NDMA contaminated valsartan products showed no association with cancer… and no evidence of a dose-response relation… In analyses of single cancer outcomes, increased risks were seen for colorectal cancer… and

[5]Plaintiffs' Motion attaches the Pottegard study as Exhibit L to the Certification of Adam M. Slater; Exhibit M to that certification is identified as the Gomm study, but the attachment is a duplicate of the Pottegard study. Both are provided here, for the Court's convenience.

> for uterine cancer… although neither these nor other single cancer outcomes reached statistical significance.

See Ex. E at pp. 3-4. Dr. Catenacci's decision to afford little weight to results that failed to achieve statistical significance is consistent with the law. Numerous courts have held non-statistically-significant results should not be given weight in a causation inquiry and dependence on such results may render an expert's opinions unreliable. *See In re Johnson & Johnson Talcum Powder Prod. Mktg., Sales, Practices & Prod. Litig.,* 509 F. Supp. at 164 (courts may also consider whether the authors of the study found the association to be statistically significant and, where the authors found an association to not be statistically significant, an opinion may be unreliable). Plaintiffs misguidedly and misleadingly cite *In re Zoloft* to suggest that statistical significance is not required. Motion at fn. 8. As the *Zoloft* opinion actually states, however, "[d]espite the problems with treating statistical significance as a magic criterion, it remains an important metric to distinguish between results supporting a true association and those resulting from mere chance." *In re Zoloft Prod. Liab. Litig,* 858 F.3d 787, 799-800 (3d Cir. 2017). The *Zoloft* court specifically declined to adopt a bright line test whether statistical significance was required ***to support an expert's opinion***, ***but affirmed the exclusion of an expert who failed*** to support her opinions with statistically significant findings. *Id.* That Dr. Catenacci gave little weight to non-significant findings is consistent with the *Zoloft* decision Plaintiffs cite.

Second, Plaintiffs claim that Dr. Catenacci minimized the positive association identified in the Gomm study between valsartan containing the NDMA impurity and liver cancer. Dr. Catenacci did no such thing — he expressly acknowledged that finding in both his report and his deposition testimony. *See* Report at p. 39 ("the analysis of individual cancer types did show a slight statistically significant association, but not causation, between NDMA-containing valsartan and liver cancer"); Ex. B (Catenacci Dep.) at 310:18-314:315:10.[6] Dr. Catenacci pointed out multiple weaknesses with the Gomm finding regarding liver cancer, including that it was not corrected for multiple testing and that it was contradicted by the fact that ***no participant*** in the Pottegard study developed liver cancer. *Id.*[7] Identifying weaknesses in a statistical study is not "uneven" or "unreliable" — it is basic and proper scientific technique. Dr. Catenacci similarly pointed out in his report that the findings of no increased risk of Gomm and Pottegard are somewhat limited by the shorter follow-up time of those papers (though that follow-up actually mirrors

[6]Dr. Catenacci also testified about what Plaintiffs tout as a supposed "inaccuracy" in his report. Specifically, there was a typo which split one sentence into two; that is not an inaccuracy and Dr. Catenacci testified that he was not trying to minimize the liver cancer finding, which he expressly called out in his Report. See Ex. B at 396:21-399:1.

[7]Notably, in their misplaced reliance on *In re Zoloft*, the language Plaintiffs omit by ellipses makes plain that statistically significant associations may be erroneous. *In re Zoloft Prod. Liab. Lit.*, 858 F.3d at 793 ("a causal connection may not exist despite the presence of significant findings").

Plaintiffs' exposure here). Report, at p. 40 ("each of these studies notes the obvious limitation of a somewhat shortened follow-up period"). Dr. Catenacci was thus entirely even handed. He pointed out limitations in the data that support his opinions and in the data that Plaintiffs' experts claim support their opinions.

Dr. Catenacci devoted nearly three pages of his Report and countless pages of his deposition testimony to describing and discussing the findings in the Gomm and Pottegard studies and what they can *and cannot* demonstrate. Plaintiffs attempt to reframe these as "concessions" about the "serious questions about the reliability" of the Pottegard study. *See* Mot. at p. 10. Of course, acknowledging that a study has limitations does not mean it is unreliable or that it has no value — it is appropriate and unbiased science. As Dr. Catenacci appropriately testified in his deposition concerning the ultimate utility of the Pottegard study: "I was asked to opine on whether or not these trace levels in these drugs were associated with known risks for cancer based on the data, this was one of the studies, and it does not show that there is evidence of an association." Ex. B at 268:13-24.

Ultimately, there was no statistically significant association demonstrated between NDMA-containing valsartan and any cancer in Pottegard and only a weak association with liver cancer (but no other cancer) in Gomm. Dr. Catenacci accurately presented these facts in his report and deposition. Plaintiffs' effort to recast this as "uneven" treatment is specious. At most, Plaintiffs have identified

(poor) grounds to cross examine Dr. Catenacci about his opinions at trial.

B. Dr. Catenacci Considered All Relevant Literature And Explained Why He Did Not Give Substantial Weight To Lesser Evidence.

The section of Dr. Catenacci's report addressing whether epidemiologic data support an association between NDMA-containing valsartan and increased cancer risk begins by explaining why the human epidemiology must be prioritized; it then explains that Plaintiffs' experts "misguidedly focus their attention extensively on less valuable dietary nitrosamine studies and animal studies of nitrosamines which, as I explain below, are only weakly related to the inquiry at issue." Report, at p. 38. Plaintiffs' Motion attempts to recast Dr. Catenacci's reasoned ranking of this evidence as a "failure to consider" mechanistic evidence and/or an "incomplete understanding" of monkey studies.

Plaintiffs improperly cite *In re Mirena* for the claim that Dr. Catenacci "ignored evidence that is highly relevant to his conclusion." Motion at 15 (citing *In re Mirena IUS Levonorgestrel-Related Prods. Liab. Litig. (No. II),* 341 F.Supp.3d 213, 242 (S.D.N.Y. 2018)). *Mirena* is inapposite and Plaintiffs' arguments are baseless. In *Mirena*, the court excluded experts for ignoring scientific standards relevant to the general causation question, offering opinions directly contradictory of those standards, and ignoring epidemiologic studies that failed to demonstrate a causal link that would support his general causation conclusion. *Id*., at 252. That is not the case, here. Dr. Catenacci plainly considered all the evidence Plaintiffs claim

he ignored; then, he rejected that evidence or placed little weight on it for reasons that are clearly and expressly set out in his Report and/or deposition testimony.

1. Dr. Catenacci Considered Mechanistic Evidence But It Is Not Material to His Opinions.

First, Plaintiffs falsely claim that Dr. Catenacci "ignored" an article entitled "Mechanisms of action of N-nitroso compounds" (Archer, M.C., Cancer, 1989). Plaintiffs concede (but minimize) that Dr. Catenacci in fact referenced that very article on his List of Materials Considered. See Mot. at p. 6; Ex. B to Report (List of Materials Considered) at p. 6. As Dr. Catenacci testified, where a scientific article was listed on his List of Materials Considered but not cited in the body of his report, it means he reviewed it, but did not find it significant enough to his opinions to reference further — not that he "ignored" it, as Plaintiffs falsely charge. Ex. B (Catenacci Dep.) at 41:6-13, 92:9-16, and 382:7-19. This is not "failure to consider known contrary evidence," (*In re Mirena,* 341 F.Supp.3d at 247) but rather, a reasoned analysis that after consideration, it was not significant to his opinions.

Importantly, plaintiffs did not ask Dr. Catenacci a single question about the so-called "mechanistic" evidence in his deposition and failed entirely to explore why it was not relevant to Dr. Catenacci's opinions. Presumably, if Plaintiffs truly believe the Archer article undermined Dr. Catenacci's opinions in some meaningful way, they would have questioned him on it. Instead, they rely on theater, claiming he failed to consider it without having asked a single question about its impact.

In the context of his broader report, though, it is plain why Dr. Catenacci did not discuss the so-called "mechanistic" evidence. The article concerns how nitrosamines are metabolized in animals and humans — namely, in the liver. Of course, such physiological studies are at the bottom of the hierarchy of epidemiologic evidence, above only unsystematic clinical observation. *In re Accutane,* 234 N.J. at 355. Regardless, Dr. Catenacci testified to the metabolism of NDMA. He also testified that he does not dispute the very point Plaintiffs emphasize in their motion — that "the biological activity of N-nitroso compounds in humans does not differ substantially from that in experimental animals." Ex. B (Catenacci Dep.) at 246:24-247:6.

Indeed, as Plaintiffs are quick to point out in their Motion, Dr. Catenacci has agreed that, based on the limited evidence available, bodies such as the International Agency for Research on Cancer (IARC) have classified NDMA and NDEA as a Group 2A (*i.e.* probable) human carcinogen. *See* Motion at p. 3. Dr. Catenacci testified to what this classification means, specifically quoting its definition that there is "limited evidence of carcinogenicity in humans and either sufficient evidence in experimental animals *or strong mechanistic evidence*…" He also pointed out that neither NDMA nor NDEA are a proven cause of human cancer. **Exhibit F** (IARC definitions); Ex. B (Catenacci Dep.) at 414:16-415:24.

Plaintiffs not only ignore Dr Catenacci's testimony and opinion that NDMA

and NDEA are not known human carcinogens, but also consistently ignore Dr. Catenacci's testimony that the relevant inquiry in this case is whether they are human carcinogens at the levels detected in valsartan over the duration the impurity existed. Ex. B (Catenacci Dep.) at 115:13-116:15 (IARC "doesn't take into account the dose and duration, which I think is an important thing to consider here"). The biological mechanisms by which NDMA and/or NDEA are metabolized in the body does not answer whether trace amounts metabolized in that fashion are carcinogenic in humans. Indeed, nothing in the Archer study addresses the carcinogenic dose of any nitrosamine or how much NDMA or NDEA the body can metabolize without any increased cancer risk.[8] See Mot. Ex. I.

Dr. Catenacci has not "ignored" mechanistic evidence — he has directly acknowledged it. This is not a "unidirectional" review of the evidence, as the court found in *In re Mirena. In re Mirena,* 341 F.Supp.3d at 251. Rather, he concluded

[8]It is also important to note that, while Dr. Catenacci knows the mechanism of nitrosamine metabolism and testified to those facts, Dr. Johnson's opinions deal directly with the metabolism of NDMA and NDEA and the levels of exposure which can metabolized completely, without any increased carcinogenic risk. Similarly, Dr. Chodosh, whose opinions Plaintiffs have not challenged, opines extensively on the mechanisms of nitrosamine metabolism and also that endogenous DNA repair processes can correct any DNA mutations caused by metabolized NDMA/NDEA. *See* **Exhibit G** (Dr. Chodosh Expert Report, "Opinions of Lewis A. Chodosh, M.D., Ph.D.") at pp. 24-26. Rule 702 does not require every expert in a case to opine on every issue.

that evidence is insufficient for him to conclude that the trace levels of NDMA present in some batches of valsartan is a human carcinogen. That is not surprising: mechanistic data is not even sufficient for IARC to conclude that NDMA is a known human carcinogen. The data are simply not important to the inquiry, here, and Dr. Catenacci's decision to consider but not to discuss the data in detail does not reflect a methodological "shortcoming." It reflects an appropriate recognition of the data's limited utility in the face of more directly relevant data.

2. Dr. Catenacci Considered Monkey Studies and Discussed Findings Relevant to His Opinions

Plaintiffs also argue that Dr. Catenacci had an "inadequate understanding" of medical literature concerning nitrosamine exposure in monkeys, based on his failure to recollect in his deposition one study identified on his List of Materials Considered but not cited in his report. Somewhat incredibly, Plaintiffs misrepresent that Dr. Catenacci was not "aware of" the study, even though it was included on his List of Materials Considered. *See* Mot. at p. 11; Ex. B to Report (Materials Considered) at p. 5 (identifying Anderson, et al., *N-nitrosodimethylamine-derived O(6) methylguanine*… (1996)).[9]

[9]Plaintiffs quote a portion of Dr. Catenacci's deposition in which he stated he was not aware of a study whose conclusions Plaintiff's counsel only vaguely described; Dr. Catenacci was not given the name of the study or its authors, nor was he informed that it was identified on his materials list. Suggesting that Dr. Catenacci must be

Further, as they did with the "mechanistic" study discussed above, Plaintiffs misrepresent the paper's ultimate findings and its importance to the actual general causation question at hand. The Anderson study did not examine whether the monkey subjects developed cancer. *See* Mot. Ex. N. Instead, the researchers looked at whether NDMA (administered at .1 mg/kg and 1mg/kg — several orders of magnitude higher doses than detected in valsartan) could induce a specific DNA adduct in monkeys and, secondarily, whether that effect was enhanced by interaction with alcohol. *Id*.

Just as with the mechanistic data, however, Dr. Catenacci's opinions are deeper than whether NDMA and/or NDEA can cause a DNA adduct which, if unrepaired and accumulating in sufficient number, could lead to cancer. As Dr. Catenacci and others (particularly Dr. Chodosh) have explained, our bodies routinely repair DNA adducts, thereby preventing cancer; the critical inquiry, not addressed by the Anderson study, is whether the levels of NDMA and/or NDEA present in valsartan are capable of overwhelming that DNA repair capacity and causing lasting mutations that might lead to cancer. *See* Ex. G (Chodosh Report) at 25; **Exhibit H** (George Johnson, "Report on NDMA/NDEA Impurities in Valsartan") at 8-10. Plaintiffs' argument that Dr. Catenacci failed to give sufficient treatment to a paper

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able to recall every study on his 54-page list of materials considered based only on counsel's description of its conclusion is absurd on its face.

that does not address the central question is meaningless. Of course, if Plaintiffs believe that some finding in the Anderson paper actually undermines any of Dr. Catenacci's conclusions, that is fodder for cross examination, not grounds to exclude his opinions under Rule 702.

3. Dr. Catenacci's Opinions About Endogenous NDMA/NDEA Formation Are Derived From Peer-Reviewed Literature Cited in His Report

As set forth in detail in his report and deposition testimony, Dr. Catenacci opines that the trace amounts of NDMA/NDEA detected in valsartan would have no discernable impact on an individual's cancer risk, even if presumed carcinogenic, because those amounts pale in comparison to the amounts produced endogenously (i.e. in the body, through natural and digestive processes). In a gross mischaracterization, Plaintiffs claim Dr. Catenacci has "no opinion" about the levels of NDMA formed endogenously, rendering his comparative opinion "unreliable." Indeed, even in the passage Plaintiffs cite, Dr. Catencci does not say he has "no opinion as to what the levels of endogenous NDMA would be inside the body" as Plaintiffs' Motion wrongly asserts. To the contrary, he expressly rejected Plaintiffs' counsel's attempt to mischaracterize his opinions in that way:

> Q. You don't have an opinion as to what the level of endogenously formed NDMA is in the human body? You don't have an opinion as to a specific level, do you?
>
> MR. INSOGNA: Object to form. Vague.

> A. ***Not other than what I've put in my report that there's a range that's very high*** compared to the question at hand here and the questions at hand, no.
>
> Q. Your opinion is that there's a potential range and that potential range may have some high figures in it, but you're not saying, "In my opinion, this is the right number," because you haven't evaluated that issue or calculated it; right?
>
> A. I'm not saying that it's one number. I'm not saying it's a potential range. ***It is a clear range that's been reported in the literature of a high very high amount and then the low end is still high compared to the levels we're talking about at the FDA level.*** There is a clear range -- not a potential range. It's a range that we see in the literature.

Ex. B at 355:24-356:20.

In passages of his deposition Plaintiffs neglect to cite, Dr. Catenacci is even more explicit: while there are various levels of endogenous NDMA formation estimated in different papers, by researchers employing different estimation techniques, ***all those levels are "much higher, on orders of magnitude, than what we're talking about*** [i.e. in valsartan]." *Id.,* at 346:22-348:11; see also 349:21-350:14 ("all of the available calculations have estimated levels far higher than the levels we're talking about here"). Specifically, Dr. Catenacci's report identifies studies that estimated levels of endogenous NDMA formation. Report, at pp. 41-42. The estimates he cites range up to 22,000 µg/day. *Id*. The Hrudey study Dr. Catenacci cites also reviews the many estimates of endogenous NDMA formation that have been published. **Exhibit I** (Hrudey, et al, "Drinking Water as a Proportion of Total Human Exposure to Volatile *N*-Nitrosamines"). As the authors conclude:

"Despite the multiple possible sources of error in the estimates of endogenous formation of NDMA we have derived, it seems clear that formation rates approaching 1 mg/day are usual and in some individuals such formation can be significantly greater." *Id*., at 2197.

Thus, despite Plaintiffs' false characterizations of his testimony, it was unnecessary for Dr. Catenacci to independently calculate endogenous NDMA formation or to select which particular estimate he found most reliable. The lowest estimate is more than 4 times greater than the highest level detected in any valsartan and the 1 mg/day level that "seems clear" in Hrudey is more than 50 times greater. In the face of that evidence, it was reasonable and reliable for Dr. Catenacci to opine that exposure to, at most, 20 µg/day of NDMA in valsartan does not increase an individual's cancer risk, because people create as much as 50 times that amount of NDMA daily within our bodies.

Ultimately, Plaintiffs' attempts to recharacterize and mischaracterize Dr. Catenacci's methodology and his prioritizing of the evidence is unavailing. Dr. Catenacci clearly explained his reasoning, which is consistent with accepted scientific methodology and the relative strength of the evidence to address the general causation inquiry at issue, here. Plaintiffs' arguments to the contrary are specious and Dr. Catenacci's opinions should not be excluded or limited.

III. PLAINTIFFS' CLAIM THAT DR. CATENACCI MADE "CONCESSIONS" INCONSISTENT WITH HIS OPINIONS IS FALSE AND NOT A BASIS FOR EXCLUSION.

Plaintiffs' other argument is a claim that Dr. Catenacci "conceded numerous points" that supposedly contradict the opinions he has offered. In several cases, however, Plaintiffs paraphrase and selectively quote Dr. Catenacci's testimony and thereby mischaracterize it. Taken in context, Dr. Catenacci's testimony is entirely consistent with his opinions. Ultimately, if Plaintiffs believe that any testimony can be used to impeach Dr. Catenacci or to undermine his opinions, that is for cross examination — it is not a ground to exclude expert testimony under Rule 702.

A. Dr. Catenacci's Testimony Is Consistent With His Opinions, And His "Concessions" Are A Fiction.

Plaintiffs' selective parsing of Dr. Catenacci's testimony is telling. Rather than undermine his opinions, when viewed in context and with the unquoted portions, Dr. Catenacci's deposition testimony makes clear that the supposed "concessions" are consistent with and supportive of his opinions and provide no grounds to question his methodology (or other ground for exclusion under Rule 702).

First, Plaintiffs mischaracterize Dr. Catenacci's deposition testimony to claim that he "agrees with IARC that NDMA and NDEA are probable human carcinogens." Mot. at p. 3, citing Ex. B (Catenacci Dep. at 115:10-12, 117:17-118:4). Throughout his deposition, Plaintiffs' counsel repeatedly attempted to extract from Dr. Catenacci a sound bite that would allow Plaintiffs to claim NDMA

and/or NDEA are probable human carcinogens ***without regard to dose***. Dr. Catenacci consistently made clear, however, that dose and duration of exposure are critical to the general causation inquiry here. Indeed, immediately between the two passages Plaintiffs' Motion selectively excerpts is this testimony:

> Q. And you don't disagree with IARC; right?
>
> A. Well, I think we're going to get into it, but maybe this is a good time to say. IARC is telling us that those -- that NDMA and NDEA are probable human carcinogens, but that doesn't take into account the dose or the duration of the exposures to these agents and that they -- ultimately they're an extrapolation from animal models, from rat models, with a lot of limitations that are quite conservative. But yes, I mean, I think we've established that IARC said that…
>
> * * * * *
>
> Q. Putting aside dose and duration, which would become relevant to determining whether a particular person claiming a particular cancer actually got cancer in whole or in part from the exposure to the NDMA in the valsartan pills -- I think that's what you're driving at; right?
>
> A. No. No, that's not – I'm not talking about that at all. I'm just saying that because it's listed as a probable carcinogen is one thing, but do have to understand that **all that's saying is that at some dose level and for some duration that it's probably carcinogenic in humans. Again, it's only probably and not definitively because it hasn't been shown in humans to have that, yet it has in some animal models, at huge doses, by the way, and for long durations that are astronomically higher than what's in this case, which is why I called it trace exposure in this case.**

Ex. B at 115:13-116:1 and 116:17-117:13. As set forth above, Dr. Catenacci also testified IARC's definition of a "probable human carcinogen" means there is

"limited evidence of carcinogenicity in humans." It is not "inconsistent" or a "concession" for Dr. Catenacci to testify that IARC has identified NMDA and NDEA as "probable" human carcinogens for which there is "limited evidence" while also consistently saying that the carcinogenic dose is the critical inquiry, here. Plaintiffs' claims to the contrary are wrong.

Second, Plaintiffs construct a strained argument that, because Dr. Catenacci co-authored a paper that identifies nitrosamines, broadly, as a risk factor associated in the medical literature with liver cancer, he has contradicted his opinion here that the levels of NDMA/NDEA in valsartan do not pose an increased risk of cancer. Mot. at p. 3. Plaintiffs do not quote Dr. Catenacci's deposition testimony or attach the relevant paper. In his deposition, Dr. Catenacci testified there are hundreds of nitrosamines and his paper discusses the class (broadly and not specifically to NDMA/NDEA), as a known risk factor associated with liver cancer: "it's an association that's been reported… we were trying to show all of the literature that's reported on various associations that have been described." Ex. B (Catenacci Dep.) at 158:9-18.[10] The paper, which Plaintiffs fail to provide this Court is attached

[10]Dr. Catenacci also testified about a similar paper which confirms the appropriate context for his identification of "risk factors." On that paper, which he co-authored for the American Society of Clinical Oncology he testified: "I think there would be probably references that nitrosamines have been reported to be associated with gastric cancer and that other reports have shown the opposite and that there's no clear consensus on those dietary studies." Ex. B at 49:4-23.

as **Exhibit J**. Critically, it has no analysis of whether any dose response exists between any nitrosamine and any form of cancer, much less an examination of whether the specific doses of the specific nitrosamines relevant here have been associated with any increased risk of cancer.[11]

Plaintiffs similarly raise a book chapter Dr. Catenacci authored about gastric cancer, misleadingly claiming he "agreed that nitrosamines are associated with gastric cancer." *See* Mot. at p. 4. His actual testimony is more precise: "I think there would be probably references that nitrosamines have been reported to associated with gastric cancer and that other reports have shown the opposite and that ***there's no clear consensus on those dietary studies***." Ex. B at 49:4-23 (emphasis added).

Neither Dr. Catenacci's testimony nor his prior paper is inconsistent with his

[11]Obviously, drugs within the same broad class (such as "nitrosamines") can have vastly different properties and bioactivity. *See, e.g., Soldo v. Sandoz Pharmaceuticals Corp.,* 244 F. Supp. 2d 434, 548-50 (W.D. Pa. 2003) (excluding expert testimony that extrapolated from findings regarding a diverse group of drugs because "evidence concerning the effect of allegedly 'similar' chemicals on the body cannot substitute for direct evidence about the drug in question"); *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1245-46 (11th Cir. 2005) ("[s]peculation replaces science" when expert ignores "differences in chemical structure" and "presumes the same effect by drugs in the same class"); *Glastetter v. Novartis Pharms. Corp.*, 252 F.3d 986, 990 (8th Cir. 2001) ("generic assumption" that drug behaves like others in its class "carries little scientific value"); *In re Abilify*, 299 F. Supp. 3d 1291, 1311 (N.D. Fla. 2018) (excluding expert testimony relying on "analogous drugs" because "reasoning by analogy" has "limited [value] in the context of establishing legal causation").

opinions here; throughout his report he cites and discusses papers that have found associations between nitrosamines and certain cancers. Report, at pp. 40-46. Critically, however, Dr. Catenacci has never stated that NDMA or NDEA are known human carcinogens or even pose an increased carcinogenic risk at the levels present in valsartan. Rather, Dr. Catenacci's opinions and deposition testimony are consistent in stating that *associations* are not the same as causation and that papers identifying such associations mostly fail to address the relevant question of dose.

Those opinions are also consistent with the science and the law. In Sir Bradford Hill's seminal paper identifying factors to consider in making causal analyses, a "strength of association" is just one factor. See **Exhibit K** Hill, A.B., *The environment and disease: association or causation?*, The Society of Medicine, May 1965 (listing 9 factors of consideration, including "strength of association"). Plaintiffs' own experts agree. See **Exhibit L** (Deposition of Mahyar Etminan, Vol. I) at 163:12-16, 165:23-166:4 ("all the causations are associations, but not all associations are causations… it's one of the criteria"); *see also* Report of Dipak Panigrahy at pp. 92-93 (identifying strength of association as one factor). Ultimately, Dr. Catenacci's prior identification of nitrosamines, broadly, as *associated* with liver cancer is entirely consistent with his opinions in this case.

Third, Plaintiffs claim that Dr. Catenacci somehow undercuts his own opinions by agreeing with statements made in the Gomm paper. Mot. p. 3. Once

again, this testimony was part of Plaintiffs' efforts to extract from Dr. Catenacci a sound bite about carcinogenic risk divorced from dose and again Plaintiffs misrepresent his testimony. Dr. Catenacci's actual testimony was as follows:

> Q. The second paragraph, the second sentence says, "NDMA is one of the most well-characterized and most potent animal carcinogens known." I want to stop there. Do you agree with that statement?
>
> A. It doesn't say anything about the dosing and stuff, but we know that at very high doses it does cause cancers in various models like rats, yes. Way –
>
> Q. I'll try again.
>
> A. Way higher than the doses that we're talking about here.
>
> Q. Yeah, but that's not what I asked you, so let's try it again. This says in the second paragraph under the introduction, "NDMA is one of the most well-characterized and most potent animal carcinogens known." Do you agree with that statement?
>
> A. I answered it with the qualification, but it does say that right there, yes.
>
> Q. And you agree with it? It's a true statement, right?
>
> A. With the qualifications, because just agreeing to that statement can be very misleading.

Ex. B at 240:21-241:24. Once again, Plaintiffs' efforts to restate Dr. Catenacci's actual testimony are telling — Plaintiffs want to remove the necessary aspect of dose from the general causation inquiry. Plaintiff's contentions also are irrelevant for Rule 702 purposes. Whether or not Dr. Catenacci agrees that NDMA is a potent

animal carcinogen at high doses has absolutely no bearing on his opinion that NDMA at the levels detected in valsartan does not increase human cancer risk.

Fourth, Plaintiffs claim that Dr. Catenacci does not dispute the carcinogenic risk to humans of ingesting NDMA-containing valsartan. See Mot. at p. 4. That is false and it is telling that Plaintiffs' Motion cites only to a portion of Dr. Catenacci's answer. In fact, the cited testimony concerned FDA's statement quantifying the supposed risk of NDMA-containing valsartan; throughout his deposition, ***Dr. Catenacci was unequivocal that NDMA and NDEA are not known human carcinogens***. Ex. B at 162:13-23 and 414:3-416:19.

Fifth, Plaintiffs claim Dr. Catenacci agrees with a conclusion by Richard Adamson from a paper entitled *The Finding of N-nitrosodimethylamine in Common Medicine* that it is important to eliminate sources of contamination in medications. Obviously, that is not a controversial proposition in any respect and in no way undermines Dr. Catenacci's opinions. More importantly, however, Plaintiffs have cherry-picked favorable language from that paper and failed to describe its ultimate conclusions. When Dr. Catenacci was given an opportunity to review the paper, he testified that it found a ***negative association*** between NDMA/NDEA and colorectal cancer and specifically found no increased risk of liver cancer. Ex. B at 411:21-414:2. Not surprisingly, Plaintiffs' counsel failed in both Dr. Catenacci's deposition and the instant motion to note the paper also states, "there is only limited clinical

evidence at present suggesting that NDMA actually causes cancer in subjects taking sartans." *See* Mot. Ex. D at p. 461. Nothing in Dr. Adamson's paper undermines Dr. Catenacci's opinions; if anything, it is supportive.

Finally, throughout their Motion, Plaintiffs make a number of untrue but ultimately irrelevant claims about Dr. Catenacci's supposed "concessions." Plaintiffs claim Dr. Catenacci has no opinion whether a study could be approved in which NDMA-containing valsartan was given to test subjects. Obviously, Dr. Catenacci is not an epidemiologist and whether such a study could be conducted has no bearing on whether NDMA/NDEA are carcinogenic at the doses at issue here.

Similarly, Plaintiffs claim that Dr. Catenacci did not assess the FDA's acceptable daily intake calculations for NDMA or calculate an alternative acceptable level. In fact, Dr. Catenacci testified that he relied on the publicly available data from FDA to assess the carcinogenic risk posed by levels of NDMA/NDEA detected in valsartan. Ex. B at 411:21-414:2. He further testified that it was unnecessary for him to calculate an alternative acceptable daily intake because the levels detected in valsartan (as found by FDA) were so much lower than ordinary human exposure to NDMA. *Id*. at 390:1-391:9. As Dr. Catenacci testified, even assuming FDA's worst-case scenario, "its at a very low level compared to the levels that we're talking about and that we saw in many of the dietary studies, just talking about the exogenous exposures that we have, let alone the endogenous exposures that we have through

just routine daily living." *Id*. In view of that opinion, there was no reason for Dr. Catenacci to calculate an alternative acceptable limit and his decision not to do so in no way undermines his opinions.

Lastly, Plaintiffs note that Dr. Catenacci did not consider internal corporate documents discussing NDMA and carcinogenicity. That is both appropriate and not inconsistent with Dr. Catenacci's opinions. As set forth above, Dr. Catenacci relied on FDA's testing data to establish the levels of NDMA/NDEA at issue. *Id*. at 411:21-414:2. Internal corporate documents and company witness testimony are not peer reviewed medical literature — indeed, if Dr. Catenacci had relied on defense witness statements about NDMA, doubtless Plaintiffs would be accusing him of bias. It was entirely appropriate for Dr. Catenacci to rely only on publicly available FDA data.

B. Dr. Catenacci's Supposed "Concessions" Are Not Grounds To Exclude Or Limit His Testimony.

As set forth above, each of Dr. Catenacci's supposed "concessions" is actually fully consistent with his ultimate opinions in this case and none undermines his opinions or renders them unreliable. Most reflect nothing more than Plaintiffs' attempt to mischaracterize Dr. Catenacci's testimony or to reframe the general causation inquiry to suit their own experts' opinions. Plaintiffs' efforts and mischaracterizations fail.

In any event, Plaintiffs do not offer a valid ground to support exclusion or even limitation of Dr. Catenacci's opinions based on these supposed "concessions."

None reflects a lack of qualifications, a methodological failure, or a lack of relevance or helpfulness, the only grounds enumerated by Rule 702. As set forth above, mere scientific disagreement between experts is also not a ground for exclusion under Rule 702. *Grace*, 455 F. Supp. 2d at 1199; *Broe*, 2016 WL 7048988 at *4.

Rather, any argument that an expert has contradicted his opinions in testimony or in writings is classic grounds for cross examination. *Broe,* 2016 WL 7048988, at *3-4 (attack focused on the expert's "internally inconsistent" report is a determination for the trier of fact); *see also Wisconsin v. Indivior Inc. (In re Suboxone (Buprenorphine Hydrochloride & Naxolone) Antitrust Litig.)*, 2020 WL 6887885, at *30-31 (E.D. Penn. Nov. 24, 2020) (expert's failure to address inconsistencies did not bear on the admissibility of her testimony and was properly tested through cross examination). The existence of grounds for cross-examination is not a basis for excluding an expert's testimony pursuant to Rule 702 and plaintiffs have urged no cognizable ground for excluding his testimony.

CONCLUSION

As Plaintiffs tacitly concede, Dr. Catenacci is extremely well qualified to opine on the issues in this case and, drawing on those qualifications, has offered relevant opinions that will be helpful for the jury. Despite Plaintiffs' claims to the contrary, each of Dr. Catenacci's opinions is well-supported by a reasoned and scientifically appropriate methodology. Plaintiffs have offered no basis to exclude

or limit Dr. Catenacci's opinions and, instead, have mischaracterized his testimony and his methodology. For those reasons as described more fully in this response, Plaintiffs' Motion should be denied and Dr. Catenacci's opinions should be admitted in their entirety.

Dated: December 1, 2021

Respectfully Submitted by the Defense Executive Committee on behalf of all Defendants,

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CERTIFICATE OF SERVICE

I hereby certify that on December 1, 2021, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system, which will send a notice of electronic filing to all CM/ECF participants in this matter.

/s/ Seth A. Goldberg
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